

Content available at: <https://www.ipinnovative.com/open-access-journals>

IP Journal of Nutrition, Metabolism and Health Science

Journal homepage: <https://www.jnmhs.com/>

Review Article

Demystifying the micronutrient deficiency burden in India

M. Mahesh¹, Jayakrishnan B², Jaidev Sudagani³, S Sridhar Mylapore⁴, B. B. Bharti⁵, Vinay Kumar Dhandhanian⁶, Soibam Pahel Meitei⁷, Srinivas Kulkarni⁸, Arindam Chatterjee⁹, Apurba Mukherjee¹⁰, Avula Laxmaiah¹¹, Ajay Kumar Singh¹², Vikas Bhutani¹³, Prabhat Goel¹⁴, Sandeep Gupta¹⁵, Puneet Saxena¹⁶, Vikas Oswal¹⁷, Ramesh Dargad¹⁸, Madhukar Rai¹⁹, Suhas Gopal Erande²⁰, Parag Shah²¹, Nikhil Bangale^{22,*}

¹JSS Medical College, JSS Academy of Health Sciences, Mysuru, Karnataka, India²Educare Institute of Dental Sciences, Malappuram, Kerala, India³Santhi Endocrine and Diabetes Hospital, Vijayawada, Andhra Pradesh, India⁴Dept. of Endocrinology and Diabetes, MIOT International, Chennai, Tamil Nadu, India⁵Patna A unit of Ford Hospital and Research Center, Patna, Bihar, India⁶Diabetes Care Centre, Orchid Medical Centre, Ranchi, India⁷Jawaharlal Nehru Institute of Medical Sciences, Imphal, Manipur, India⁸Mahavir Hospital & Research Centre, Hyderabad, Telangana, India⁹New Hospital Road, Birbhum, West Bengal, India¹⁰R. G. Kar Medical College and Hospital, Kolkata, West Bengal, India¹¹JCMR - National Institute of Nutrition, Secunderabad, Telangana, India¹²Medigram The Superspecialty Hospital, Saharanpur, Uttar Pradesh, India¹³Fortis Hospital, Punjab, India¹⁴Dr. Prabhat Goel Clinic, Gurugram, Haryana, India¹⁵Luthra Hospital and Research Centre, Bilaspur, Chhattisgarh, India¹⁶S M S Medical College and Hospital Jaipur, Asha Clinic, Jaipur, Rajasthan, India¹⁷DPS Shatabdi Municipal Hospital, Mumbai, Maharashtra, India¹⁸Lilavati Hospital and Research Centre, Mumbai, Maharashtra, India¹⁹Institute of Medical Sciences BHU, Varanasi, Uttar Pradesh, India²⁰Akshay Hospital, Pune, Maharashtra, India²¹Gujrat Endocrine Centre, Ahmedabad, Gujarat, India²²Head Medical Affairs- Bayer Consumer Health, Mumbai, Maharashtra, India

ARTICLE INFO

Article history:

Received 15-07-2022

Accepted 25-07-2022

Available online 09-09-2022

Keywords:

Micronutrient Deficiency

Hidden Hunger

Immunostimulation

Immunoregulation

ABSTRACT

More than two billion people suffer from micronutrient deficiencies (MiNDs) globally, with nearly half living in India. The current risk of ‘hidden hunger’ is severe in India due to serious deficiency risks across an array of essential micronutrients. A nationwide advisory board meeting attended by more than 20 Indian health care professionals (HCPs) was conducted to determine their clinical viewpoint on MiND. An in-depth search of PubMed studies emphasizing various aspects of MiND relevant to the Indian scenario was performed and presented to eminent HCPs from across India who then shared their opinions and perspectives based on their clinical experiences associated with MiND.

This is an Open Access (OA) journal, and articles are distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License](https://creativecommons.org/licenses/by-nc-sa/4.0/), which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprint@ipinnovative.com

1. Introduction

Hidden hunger, also known as micronutrient deficiencies (MiNDs), is the umbrella term used to represent the lack of essential vitamins and minerals required from the diet to sustain virtually all normal cellular and molecular functions.¹ The World Health Organization (WHO) has defined ‘micronutrients’ as compounds required in very small amounts (< 100 mg/day).² More than one-in-three individuals are deficient in one or more micronutrients worldwide.³ Coexistence of multiple MiNDs commonly occurs worldwide.¹ India is undergoing an enormous nutrition transition as MiND has reached its alarming peak in a large mass of Indians irrespective of them being in overweight and underweight states, as supported by scientific evidence.² Hence, we aimed to understand the Indian clinical viewpoint of MiND, its various causes, the rationale behind the usage of multivitamin supplements, and whether these supplements ameliorate any physical symptoms of MiND, or improve immunity and increase energy for daily well-being.

2. Discussion

Relevant aspects of MiND with support of PubMed literature and clinical evidence were presented to HCPs who then shared their clinical recommendations and provided their consensus associated with MiND.

2.1. MiND or hidden hunger

MiNDs are also termed as ‘Hidden Hunger’, as subnormal levels of certain vitamins and minerals can increase general morbidity and mortality without any obvious clinical symptoms or signs to suggest deficiency.⁴ In contrast to macronutrients, micronutrients are required only in small quantities, but are essential for physical and mental functioning as even mild to moderate MiNDs can affect a person’s well-being and mental functioning.^{3–5} Unlike energy-protein undernourishment, health impacts of MiND are not always acutely visible; thus termed ‘hidden hunger’.³

According to a nationwide survey of HCPs, severe MiNDs are particularly reported within a few days in hospitalized patients (while refusing food along with the illness and medications) mainly after gastrointestinal surgeries which contribute heavily to overall disease outcomes. However, MiND is not necessarily reported only in a disease state, but is prevalent and is bound to have a negative impact on an apparently healthy individual as well. All the health care professionals (HCPs) agreed that it is clinically challenging to identify or screen MiNDs due to the non-specific symptoms observed in healthy adults which has further led to its more alarming rise. Around 90%

HCPs strongly agreed that MiNDs further increase the risk of other diseases like diabetes, hypertension, osteoporosis, asthma, depression, neurological disorders, cardiovascular disorders, endocrine disorders, etc. in healthy adults.

2.2. Prevalence of MiND in India

More than two billion people suffer from MiND globally, with nearly half living in India.³ Current risk of ‘hidden hunger’ is severe in India due to serious deficiency risks across an array of essential micronutrients. Results suggest a widespread (> 80% total Indian population) risk of deficiencies in calcium, vitamin A, B12, and folate, with more localized deficiencies in iron, zinc, and vitamin B6.³ The prevalence of serum zinc deficiency in India is > 20%, which indicates a public health significance. The Indian Council of Medical Research (ICMR) also reports that lower levels of plasma magnesium and zinc and reduced zinc/copper ratio are associated with coronary artery disease in Indians. A survey conducted by National Nutrition Monitoring Bureau (NNMB) showed milder grades of vitamin A deficiency causing night blindness and Bitot’s spots. Despite sunlight exposure throughout the year, a high prevalence of vitamin D deficiency in different population groups including adults has been demonstrated by several Indian studies. Vitamin D deficiency and low intake of calcium are responsible for the high prevalence of osteoporosis particularly in Indian women.⁶ The Indian females also have high MiNDs due to less consumption of nutrients than males in their diet ($p < 0.001$).⁷ A community-based cross-sectional study showed a significantly lower intake of vitamins A, B1, B2, B3, B12, zinc, folate, and iron in Indian women than men.⁸ Another cross-sectional Indian survey reported a large percentage of pregnant women had less than 50% of the recommended intakes of iron, calcium, and folic acid (81%, 77%, and 96%, respectively).⁹ According to the HCPs, the micronutrient diet intake of the urban Indian population is below than recommended dietary allowance (RDA). MiND is highly prevalent in >62% of urban and semi-urban adults due to wrong eating habits, inadequate diet, and prevalence of anemia leading to the inadequacy of multiple micronutrients.

2.3. Causes of MiND

Micronutrient intakes vary significantly between diet inadequacy, Indian dietary patterns, losses due to food processing/cooking, and food impurities (Table 1).^{10–12} Insufficient micronutrient intakes, can be due to several reasons such as the changing Indian dietary patterns prompted by a host of factors including agricultural, economic, lifestyle, health and nutrition transitions, increased micronutrient requirements not met during pregnancy and lactation, diseases, advancing age,

* Corresponding author.

E-mail address: nikhil.bangale@bayer.com (N. Bangale).

infections, or surgery.⁶ Even ‘healthy’ individuals are at risk of MiND due to sedentary behavior, and lifestyle-related factors. In short, a bidirectional relationship exists among nutrition, infection, and immunity as changes in one component consequently affect the others.^{10–12}

Table 1: Causes of inadequate micronutrient intake via poor diets.

Causes	Causative features
Daily diet inadequacy	<ul style="list-style-type: none"> • Due to reduced bioavailability in plant sources, vegetarian diets provide an inadequate nutritional intake of omega-3 fatty acids, vitamin B12, and minerals. • Insufficient intake owing to the weight-reducing and imbalanced diets, and wrong dietary and modern eating habits. • Increased consumption of junk food leads to unhealthy snacking habits Eating disorders, emotional and/or physiological stress.
Micronutrient loss in food	Farming techniques and food processing results in plant micronutrient loss Cooking leads to a loss of vitamins (25%-40%).

More than 90% HCPs strongly agreed that increased micronutrient requirements are not met during pregnancy and lactation, in various diseases, lifestyle-related stress, nutrient-nutrient interactions, infections, or post-surgery. Malabsorption syndrome, vitamin B12 hypovitaminosis, and chronic use of medications/antibiotics adversely affect the gut microbiota and can consequently cause MiND. They also conceded that insufficient intake due to weight-reducing diets, imbalanced diet, and wrong dietary/cooking/eating habits are strong contributing factors to MiND in urban Indians.

2.4. Consequences of MiND across the life span

Inadequate intake of micronutrients at any stage of life is a vicious cycle affecting various functions within the immune system, manifesting in decreased resistance to infections, and an increase in severity of symptoms (Figure 1).¹³

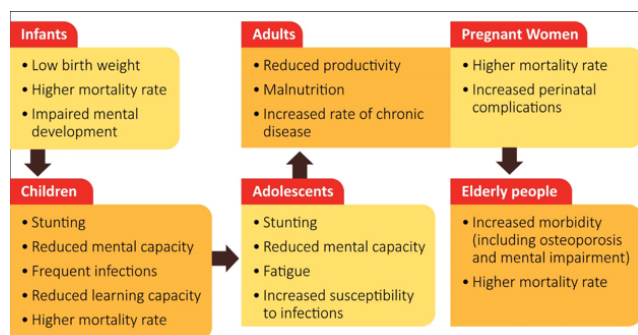


Fig. 1: Consequences of micronutrient inadequacies across the age groups.

Of greatest concern is the fact that the vicious cycle of MiNDs is associated with adverse consequences throughout an individual’s life span perpetuating across the generations, with far-reaching consequences on the future population.¹³

2.5. Clinical outcomes of MiND

Before clinical symptoms of deficiency (lack of energy and increased vulnerability to infections) appear, MiNDs develop progressively through several sub-clinical stages (Figure 1).^{11,14}

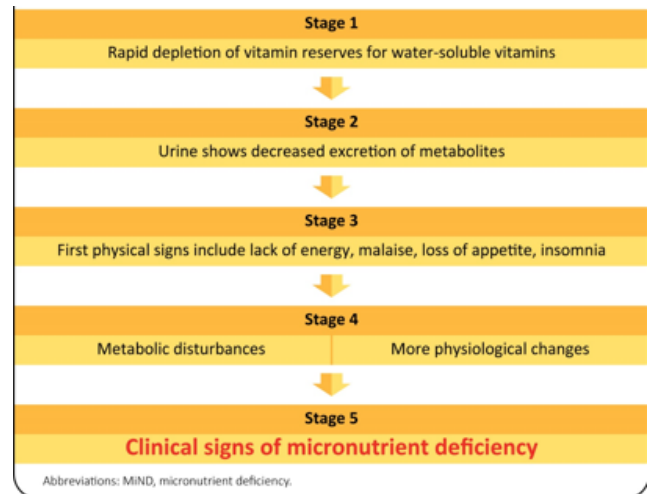


Fig. 2: Sub-clinical stages of mind

Majority of the HCPs agreed that micronutrients have a strong impact at molecular and cellular levels and manifestations of fatigue and reduced immunity may occur when supplies of these micronutrients are inadequate. When the patient develops clinical signs, it is likely that MiND is already being established as the deficiencies start three to six months prior. For instance, dementia can be the first clinical sign of iron deficiency, vitamin B12 deficiency can lead to neurological disorders, folic acid deficiency can lead to hematological disorders, and vitamin D deficiency can cause muscle weakness, bone pain, and fatigue.¹⁵

2.6. Inadequacy of daily diet to fulfill RDA of micronutrients

The ICMR advocates that RDAs are daily dietary nutrient intake levels that would be sufficient to meet the nutrient requirements of nearly all healthy individuals in a particular life stage and gender group.⁶ However, reports of the National Nutrition Monitoring Bureau are alarming as several micronutrient intakes of 70% Indian population are less than 50% of the RDA. Agrawal et al. evaluated 502 Indian urban OPD patients visiting for their routine follow-ups to assess the level of micro and macronutrient consumption among the study participants and their

comparison with the current RDA recommendation. The study outcomes showed that among micronutrients, consumption of calcium, copper, iron, magnesium, zinc, and vitamin B12 are below RDA guidelines in the Indian population.⁷ The ICMR also reports that iron deficiency in the diet is the main cause of anemia in all age groups and that the median risk of inadequate intake of iron is in the range of 48%-78%.⁶ Based on the health survey responses of 220 HCPs in urban India (Mar-Apr 2021), nearly 85% of Indian doctors (GPs, ENTs, Internal Medicine experts), and 93% of Indian nutritionists also believe that only 70% (or even lower) of our micronutrient requirements are fulfilled by our daily Indian diet in urban adults aged 25-45 years.¹⁶ Majority of the HCPs agreed that among micronutrients, consumption of calcium, iron, folic acid, zinc, vitamin D3, and B12 are below RDA guidelines in the Indian population. Among MiNDs, iron deficiency anemia, vitamin A deficiency, and riboflavin deficiency are highly prevalent in the Indian population.

2.7. Important micronutrients to enhance immunity

Scientific evidence suggests that zinc, vitamin A, vitamin C, and vitamin D are few of the most important micronutrients to enhance immunity, thus influencing the risk and clinical course of viral respiratory infections (Table 2).¹⁷ Although, no single vitamin can work on its own for enhancing immunity; however multivitamins can definitely work in combination and in synergy for improving immunity by helping each other in multiple chain reactions, in the respiratory chain cycles, and in various stages of development of immunity.¹⁷

An adequate micronutrient intake is essential to aid recovery from infection, which may be difficult because food intake may decrease during illness, and antibiotic use can also deplete certain micronutrients. An immune response is likely to be impaired when micronutrient levels are insufficient. Supplementation with multiple micronutrients (MMN) may have significant benefits on immune cells and responses.¹⁸ To achieve optimal micronutrient intake for immune defenses through a well-balanced and diverse diet alone is difficult, especially for micronutrients such as vitamins C and D, which need to be taken in doses higher than the RDA to be immune effective.¹⁹

2.8. Plugging the daily gap of MiND with multivitamin/mineral supplements

Considering the active role of micronutrients in immunity, there is a rationale for micronutrient supplementation to restore concentrations to recommended levels, especially after an infection, and during the recovery, phase to support immune function and its maintenance.¹⁷

Vitamin A supplementation is correlated with reducing infection-related morbidity and mortality associated with vitamin A deficiency.¹⁷ WHO/UNICEF recommend zinc supplementation during diarrheal infection and for the treatment of severe malnutrition.⁶ A systematic review and meta-analysis study has shown a borderline significant preventive effect of micronutrient supplementation (vitamin A, B12, C, D, iron, and zinc) against the incidence of viral respiratory tract infections (RTIs). The prevention of viral RTIs occurs through micronutrient supplementation due to the recognized role of micronutrients in immune function.²⁰ For instance, supplementation with zinc was found to lower the frequency and severity of infections like diarrhea and pneumonia and reduce mortality. On the other hand, attaining peak bone densities is essential to prevent osteoporotic fractures in later life. Vitamin D and calcium supplementation have demonstrated beneficial effects by attaining peak bone densities during the growth phase and in adults for preventing osteoporosis.⁶ More than 90% HCPs agreed that micronutrient supplementation can be used as a supportive therapy, especially during the recovery phase after an infection or surgery. On the other hand, few HCPs clarified that it is a misconception that only thin and fragile people who are malnourished are nutritionally deficient. In fact, obese patients have more nutritional deficiencies. For instance, vitamin D deficiency is one of the main causative factors of obesity. In short, obese people also require micronutrient supplementation. Moreover, the elderly due to gastrointestinal tract (GIT) absorption issues, and patients with diabetes, hypertension, chronic obstructive pulmonary disease (COPD), asthma, or cardiovascular diseases are also micronutrient deficient and in need of micronutrient supplementation. A recent study demonstrated that supplementation of folic acid alone or in combination with vitamin B12 to Indian patients with vascular disease had reduced the observed elevated homocysteine levels. Further, chronic and severe forms of folate deficiency leading to abnormal hemopoiesis and megaloblastic anemia (MBA), promptly responds to folate supplementation. Compelling evidence suggests that vitamin C supplementation decreases the risk of cardiovascular accidents and asthma, prevention of cataracts, and its impact on the common cold.⁶

2.9. Impact of multivitamin/mineral supplementation on immunity/energy/cognition

Considering the importance of micronutrients in immunity, there is a rationale for micronutrient supplementation to restore concentrations to recommended levels, especially after an infection, and to support immune function and maintenance (Table 3).¹⁷

Clinical data suggest that vitamin C supplementation reduced the episodes of upper RTIs in swimmers, lowers the risk of pneumonia, and decreases the duration and

Table 2: Mechanism of action of vitamins A, C, D, & zinc in supporting immune response.

In the Inflammatory and innate immune response	In the adaptive immune response
<p>Vitamin A Integrity of epithelia Differentiation and function of NK cells Promotion of Foxp3+ Treg generation Inhibition of Th1/Th17 generation Phagocytic and oxidative burst activity of macrophages Secretion of the pro-inflammatory cytokines IL-12 and IL-23</p> <p>Vitamin C Barrier integrity Scavenger of ROS Chemotactic ability and antibacterial activity of neutrophils Apoptotic process of neutrophils Reduction of formation of NETS</p> <p>Vitamin D Production of antimicrobial peptides.</p> <p>Modulation of macrophages/monocytes and dendritic cell functions. Limits the over production of pro-inflammatory cytokines from macrophages (IL, TNF-α)</p> <p>Zinc Maintenance of membrane barrier integrity. Direct antiviral effects. Decreases oxidative stress.</p>	<p>Vitamin A Growth and differentiation of B cells Production of antibodies and immunoregulatory function of Treg cells</p> <p>Vitamin C Differentiation and proliferation of B and T cells Immunostimulator of antibody production (IgM and IgG) T cell maturation via epigenetic mechanisms</p> <p>Vitamin D limits the over production of pro-inflammatory cytokines from T cells (INF-γ, IL-2, IL-8, and IL-6). Th1 to Th2 shift, increases Th2 cytokines (IL-4, IL-10). Induces differentiation of Treg cells. Reduces excessive antibody production.</p> <p>Zinc Limits excessive release of Pro-inflammatory cytokines (IL-2, IL-6, and TNF-α) Enhances the number of Treg cells.</p> <p>Omega 3 FA [Specialized pro-resolving mediators (SPMs)] Treg cell formation and B cell activation Upregulates CCR5 expression</p>

Abbreviations: NK, natural killer; Foxp3+, Forkhead box p3; IL, interleukin; Treg, regulatory T cell; Th, T helper cell; ROS, reactive oxygen species; NETS, neutrophil extracellular traps; TNF- α , tumor necrosis factor- α ; Ig, immunoglobulin; FA, fatty acid.

Table 3: Impact of multivitamin/mineral supplementation on immune function.

Micronutrient	Impact of supplementation on immune functions
Vitamin C	High doses stimulate phagocytic and T-lymphocytic activity. Antioxidant properties to combat oxidative stress. Aids in wound healing.
Vitamin D	Calcitriol restores the immune function of macrophages. Increased resistance to infection especially RTIs.
Zinc	Beneficial effects on intestinal immune functions Increases cytotoxicity of NK cells Restores thymulin activity Reduces the number of activated T helper cells (which can contribute to autoimmunity)
Vitamin A	Retinoic acid modulates specific microbiota in the gut Helps reverse adverse effects on immune functions of neutrophils, eosinophils, NK cells, and macrophages Improves antibody titer response to vaccines
Iron	Improves intracellular microbial killing and cellular immunity
Copper	Increased ability of neutrophils to engulf pathogens
Selenium	Improves cell-mediated immunity Improves T helper cell counts Enhances immune response to viruses in deficient individuals
Magnesium	Reduces oxidative damage to DNA of peripheral blood lymphocytes in athletes and sedentary young men. Reduces leukocyte activation.

symptoms of cold. Three clinical studies showed a > 80% lower incidence of pneumonia in the vitamin C groups, supporting the potential role of vitamin C in reducing the risk of pneumonia, particularly in individuals with low plasma vitamin C levels. Furthermore, regarding the effect of vitamin C in treating pneumonia, in older patients, lower mortality and reduced severity of disease were found in the vitamin C group, particularly in the most ill patients.¹⁷ On the other hand, vitamin D supplementation showed a significant beneficial effect in decreasing the risk of experiencing at least one acute RTI by exhibiting protective effects.²¹ It has been reported during influenza A infection that interferon- β (IFN- β), tumor necrosis factor (TNF)- α , IL-8, and IL-6 in the lungs were reduced in response to treatment with vitamin D. On the other hand, during respiratory syncytial virus infection, the nuclear factor kappa B (NF- κ B) inhibitor was induced in response to treatment with vitamin D.¹⁷ Moreover, zinc supplementation reduced the duration and incidence of symptoms in common cold and RTIs. Zinc supplementation was also effective in decreasing oxidative stress and was found to have direct antiviral effects. Zinc supplementation for more than three months also significantly reduced the frequency and severity of diarrhea and respiratory illnesses.^{6,22}

A prospective study showed significant improvement in superoxide dismutase (SOD) action and a significant decrease in fatigue ($p = 0.0009$), sleep disorders ($p = 0.008$), autonomic nervous system symptoms ($p = 0.018$), frequency and intensity of headaches ($p = 0.0001$) with a multivitamin/mineral supplement treatment for two months. Thus, multivitamin/mineral supplementation can safely diminish fatigue symptoms by improving antioxidant status.²³ Another placebo-controlled, double-blind, and randomized study showed significant attenuation of increased ratings of physical tiredness on day 62 assessments ($p < 0.05$) and a significant decrease in levels of homocysteine ($p = 0.006$). There was also an increased accuracy across the entire multi-tasking framework and performing specific tasks (Mathematical Processing, Stroop Color-Word). Thus, there was a significant improvement in physical tiredness engendered by task performance and significant improvement in cognitive function following 62 days of treatment with multivitamin/mineral supplementation in females.²⁴

Scientific data has proved that supplements with micronutrients reduced fatigue (vitamins B1 and D, iron), increased activity and feelings of being energetic (vitamin B1), increased muscle endurance (zinc), improved exercise tolerance (magnesium) and physical capacity/performance [coenzyme Q10 (CoQ10)], and improved physical recovery (CoQ10). A positive association was noted between well-being and the feeling of being clearheaded and composed (vitamin B1) and on symptoms of seasonal affective

disorder, including depression (vitamin D).²⁵

The HCP consensus agreed that there is a rationale for prescribing micronutrient supplementation to fulfill micronutrient deficiencies in patients.

2.10. Impact of multivitamin/mineral supplementation on fulfilling MiNDs (as per RDA in daily diet)

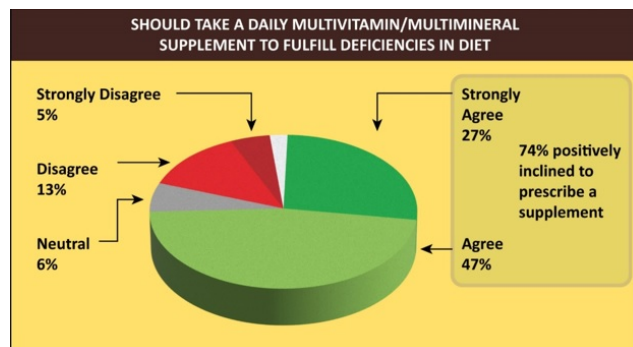


Fig. 3: Abbreviations: HCP, health care professional; MiND, micro nutrient deficiencies; RDA, recommended allowance.

HCP Urban survey impact of multivitamin/mineral supplementation on fulfilling Mind (as per RDA) in daily diet.

Based on the health survey responses of 220 HCPs in urban India (Mar-Apr 2021), 74% of Indian doctors/nutritionists are positively inclined to prescribe multivitamin/mineral supplements to fulfill micronutrient deficiencies (as per RDA) in daily Indian diet (Figure 3).¹⁶

2.11. Benefits of natural or herbal ingredients to boost immunity

Attacks of viruses and bacteria can be counteracted with an efficient immune system and thus, stimulation of the body's defense mechanism against infections is an effective approach. Compelling evidence suggests that natural/herbal ingredients stimulate and help in maintaining a healthy immune system. Natural/herbal ingredients modulate immune functions by immunostimulation/immunoregulation for the control and prevention of infections. It is postulated that a stimulated immune system fights better against any impending infections and exerts indispensable effects on stress- and infection-induced immunosuppression. Based on in vitro and animal studies, natural/herbal ingredients (turmeric, Shatavari, giloy, amla, and tulsi) modulate immune functions by immunostimulation/immunoregulation for the control and prevention of infections (Table 4).²⁶ The positive effect of tulsi was demonstrated by the increased immune response with increased natural killer (NK) and T-helper cells, less fatigue, reduced creatine kinase, improvement in cognitive flexibility, short-term

Table 4: Pharmacological properties of natural ingredients.

Natural Ingredients	Pharmacological Properties of Natural Ingredients
Tulsi ^{21,26}	Adaptogenic, immunomodulatory, antimicrobial, cardioprotective, anti-inflammatory, antiviral, antifungal, antibacterial, and hepatoprotective actions Enhances the immune response by phagocytic activity and index with a rise in the lymphocyte count, neutrophil count, and antibody titer
Turmeric ^{26,27}	Anti-inflammatory activity of curcumins in both acute/chronic cases of inflammation Potent antioxidant to lower lipid peroxidation in cells by sustaining activities of antioxidant enzymes (catalases, superoxide dismutase, and glutathione peroxidase) at higher levels
Ashwagandha ²⁶	Anti-inflammatory, antitussive, and antioxidant agent Enhances nitric oxide (NO) synthase activity of macrophages to increase their microbe killing power Stimulatory effect on the immune system, enhances antibody and red blood cell levels, and increases the number of white blood cells to destroy germs Marked increase in the primary and secondary antibodies and also a cell-mediated immune response to possess immunostimulatory properties
Shatavari ^{26,28,29}	Antioxidant, immunomodulatory, anti-inflammatory, anti-bronchitis, antidyspepsia, and potential broad-spectrum antibiotic properties
Giloy ^{26,30}	Boosts the immune system by immunomodulatory and cytoprotective activities through augmentation of antibody production and various non-specific immune mechanisms
Amla	Antimicrobial, antiviral, antioxidant, anti-inflammatory, immunomodulatory, larvicidal, cardioprotective, and wound healing activities. Interferes with the adhesion of <i>Candida albicans</i> to buccal epithelial cells and denture acrylic surfaces in vitro. Antimicrobial effect by inhibiting adhesion and synergistic increase in zone of inhibition against <i>Staphylococcus</i> with amoxicillin by agar diffusion and disk diffusion methods. Significant reduction in mean colony count of <i>Escherichia coli</i> , <i>Staphylococcus aureus</i> , and <i>Klebsiella pneumoniae</i> by tube dilution method.

memory, and attention and reductions of 31.6%–39% in overall stress-related symptoms in psychosomatic problems.³¹ Administration of turmeric is associated with a reduction in recurrent respiratory tract infections due to beneficial immune-modulatory effects.²⁷ In vivo effects of Shatavari on effector T cell immunity suggest its use in respiratory infections where broader stimulation of T-helper type 1 (Th1) and Th2 immunity supports its immunoadjuvant potential.²⁸ The broad-spectrum antibacterial pattern in amla extract showed superior effects against drug-resistant and multidrug-resistant infections.²⁹ The immunomodulatory properties of giloy have demonstrated activity in a wide range of chronic inflammatory disorders such as diabetes and cognitive decline.³⁰

The HCP consensus conceded that although natural/herbal ingredients have multiple pharmacological benefits, there's a need for extensive clinical evaluation.

3. Summary

India is undergoing an enormous nutrition transition as MiND has reached its alarming peak in a large mass of Indians irrespective of whether they are in overweight or underweight states. MiND is highly prevalent in urban India. 'Hidden Hunger' or MiNDs are subnormal levels of vitamins and minerals that can increase general morbidity

and mortality without any obvious clinical symptoms or signs to suggest deficiency. MiNDs further increase the risk of diabetes, hypertension, osteoporosis, asthma, depression, neurological disorders, cardiovascular disorders, endocrine disorders, etc. in healthy adults. However, MiND is not necessarily reported only in a disease state, but it is bound to have a negative impact on healthy adults as well.

Serious deficiency risks are reported across most essential micronutrients (calcium, iron, magnesium, zinc, and vitamin B12) in India. The Indian females also have high micronutrient deficiencies due to less consumption of nutrients than males in their diet. Reports of the National Nutrition Monitoring Bureau are alarming as several micronutrient intakes of 70% Indian population are below 50% RDA. Micronutrient intakes vary significantly among Indian dietary patterns, diet inadequacy due to an imbalanced diet, wrong dietary habits, modern eating habits, increased consumption of junk food, and unhealthy snacking habits. Inadequate intake of micronutrients at any stage of life is a vicious cycle affecting various functions within the immune system, manifesting in decreased resistance to infections, and an increase in severity of symptoms. Before clinical symptoms of deficiency appear, MiNDs develop progressively through several sub-clinical stages consequently leading to a lack of energy and increased vulnerability to infections. Scientific evidence suggests that zinc, vitamin A, vitamin C, and vitamin D

are a few of the most important micronutrients to enhance immunity, thus influencing the risk and clinical course of viral respiratory infections. There is a rationale for regular consumption of micronutrient supplementation as a preventive role or to restore concentrations to recommended levels. Micronutrients increase energy levels, reductions in physical and mental fatigue, improvements in concentration, mental stamina, and mood, and reductions in feelings of depression, anxiety, and stress.

Compelling evidence suggests a significant preventive effect of micronutrient supplementation (vitamin A, B12, C, D, iron, and zinc) against the incidence of viral respiratory tract infections. It is a misconception that only thin and fragile people who are malnourished are nutritionally deficient. In fact, obese patients have more micronutrient deficiencies and are in urgent need of micronutrient supplementation. Moreover, healthy elderly or those with comorbidities are also micronutrient deficient and in need of micronutrient supplementation. There is a strong rationale for prescribing micronutrient supplementation to fulfill micronutrient deficiencies to treat patients with disease states as well as to prevent the incidence of several respiratory infections in healthy adults. Several trials that evaluated the effects of MMS in healthy populations have shown that it has clinically-proven beneficial effects on energy, cognitive performance, and well-being.

Natural/herbal ingredients modulate immune functions by multiple pharmacological effects for the control and prevention of infections. It is postulated that a stimulated immune system fights better against any impending infections and exerts indispensable effects on stress- and infection-induced immunosuppression. Based on in vitro and animal studies, natural/herbal ingredients (turmeric, Shatavari, ashwagandha, giloy, amla, and tulsi) modulate immune functions by immunostimulation/immunoregulation for the control and prevention of infections.

4. Source of Funding

None.

5. Conflict of Interest

None.

Acknowledgements

Unrestricted educational grant supported by Bayer India. Manuscript and editorial support by Insignia Communication Pvt Ltd. Mumbai.

References

- Bailey R. The Epidemiology of Global Micronutrient Deficiencies. *Ann Nutr Metab.* 2015;66(2):22–33.
- Venkatesh U, Sharma A, Ananthan VA. Micronutrient's deficiency in India: a systematic review and meta-analysis. *J Nutr Sci.* 2021;10:110.
- Ritchie H, Reay DS. Projecting and Addressing India's Hidden Hunger. *Front Sustain Food Syst.* 2018;2:11.
- Schiavo L. Micronutrient Deficiencies and Sleeve Gastrectomy for Weight Reduction; 2013. Available from: <https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/micronutrient-deficiency>.
- Lowe NM. The global challenge of hidden hunger: perspectives from the field. *Proc Nutr Soc.* 2021;80(3):283–9.
- Recommended Dietary Allowances and Estimated Average Requirements Nutrient Requirements for Indians - 2020, A Report of the Expert Group Indian Council of Medical Research National Institute of Nutrition; 2020. Available from: https://www.im4change.org/upload/files/RDA_short_report%281%29.pdf.
- Agrawal N. Study of dietary intake of micro and macronutrients and comparison with the Recommended Daily Allowance (RDA). *J Nutr Metab Health Sci.* 2020;3(1):10–2.
- Shalini T, Sivaprasad M, Balakrishna N. Micronutrient intakes and status assessed by probability approach among the urban adult population of Hyderabad city in South India. *Eur J Nutr.* 2019;58(8):3147–59.
- Sharma S, Akhtar F, Singh RK. Dietary Intake across Reproductive Life Stages of Women in India: A Cross-Sectional Survey from 4 Districts of India. *J Nutr Metab.* 2020;23:9549214.
- Rizzo NS, Siegl KJ, Sabate J, Fraser GE. Nutrient profiles of vegetarian and nonvegetarian dietary patterns. *J Acad Nutr Diet.* 2013;113(12):1610–9.
- Huskisson E, Maggini S, Ruf M. The role of vitamins and minerals in energy metabolism and well-being. *J Int Med Res.* 2007;35(3):277–89.
- Shridhar K, Dhillon PK, Bowen L, Kinra S, Bharathi AV, Prabhakaran D. Nutritional profile of Indian vegetarian diets—the Indian Migration Study (IMS). *Nutr J.* 2014;13:55.
- Maggini S, Pierre A, Calder PC. Immune Function and Micronutrient Requirements Change over the Life Course. *Nutrients.* 2018;10(10):1531.
- Combet E, Buckton C. Micronutrient deficiencies, vitamin pills, and nutritional supplements. *Principles Hum Nutr.* 2015;43(2):66–72.
- Briani C. Cobalamin Deficiency: Clinical Picture and Radiological Findings. *Nutrients.* 2013;5(11):4521–39.
- Madhari RS, Boddula S, Ravindranadh P, Jyrwa YW, Boiroju NK. High dietary micronutrient inadequacy in peri-urban school children from a district in South India: Potential for staple food fortification and nutrient supplementation. *Matern Child Nutr.* 2020;16(3):e13065.
- Pecora F, Persico F, Argentiero A, Neglia C, Esposito S. The Role of Micronutrients in Support of the Immune Response against Viral Infections. *Nutrients.* 2020;12(10):3198.
- Gombart AF, Pierre A, Maggini S. A Review of Micronutrients and the Immune System-Working in Harmony to Reduce the Risk of Infection. *Nutrients.* 2020;12(1):236.
- Marcos A. A Review of Micronutrients and the Immune System-Working in Harmony to Reduce the Risk of Infection. *Nutrients.* 2021;12(1):4180.
- Boerstra BV, De Jong N, Meyer R. Nutrient supplementation for prevention of viral respiratory tract infections in healthy subjects: A systematic review and meta-analysis. *Allergy.* 2022;77(5):1373–88.
- Martineau AR, Jolliffe DA, Hooper RL. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ.* 2017;356:6583.
- Gammoh NZ, Rink L. Zinc in Infection and Inflammation. *Nutrients.* 2017;9(6):624.
- Maric D, Brkic S, Tomic S, Novakovmikić A, Cebovic T, Turkulov V. Multivitamin mineral supplementation in patients with chronic fatigue syndrome. *Med Sci Monit.* 2014;20(1):47–53.
- Haskell CF, Robertson B, Jones E. Effects of a multi-vitamin/mineral supplement on cognitive function and fatigue during extended multi-tasking. *Hum Psychopharmacol.* 2010;25(6):448–61.
- Maggini S, Ovari V, Gimenez F, Pueyoalaman I. Benefits of micronutrient supplementation on nutritional status, energy

- metabolism, and subjective wellbeing. *Nutr Hosp.* 2021;38(2):3–8.
26. Tiwari R, Latheef SK, Ahmed I. Herbal Immunomodulators - A Remedial Panacea for Designing and Developing Effective Drugs and Medicines: Current Scenario and Future Prospects. *Curr Drug Metab.* 2018;19(3):264–301.
 27. Gupta SC, Patchva S, Aggarwal BB. Therapeutic roles of curcumin: lessons learned from clinical trials. *AAPS J.* 2013;15(1):195–218.
 28. Gautam M, Saha S, Bani S. Immunomodulatory activity of Asparagus racemosus on systemic Th1/Th2 immunity: implications for immunoadjuvant potential. *J Ethnopharmacol.* 2009;121(2):241–8.
 29. Khurana S, Tiwari R, Sharun K. Emblica Officinalis (Amla) with a Particular Focus on its Antimicrobial potentials: A Review. *J Pure Appl Microbiol.* 2019;13(4):1995–2012.
 30. Yates CR, Bruno EJ, Yates ME. Tinospora Cordifolia: A review of its immunomodulatory properties. *J Diet Suppl.* 2022;19(2):271–85.
 31. Jamshidi N, Cohen MM. The Clinical Efficacy and Safety of Tulsi in Humans: A Systematic Review of the Literature. *Evid Based Complement Alternat Med.* 2017;2017:9217567.

Author biography

M. Mahesh, Professor in Medicine and Unit Head

Jaykrishnan B, Professor Department of Medicine and Unit Head

Jaidev Sudagani, Consultant Endocrinologist

S Sridhar Mylapore, Head of the Department of Endocrinology and Diabetes

B. B. Bharti, Consultant Cardiologist & Interventionist

Vinay Kumar Dhandhanian, Consultant Diabetologist & Metabolism

Soibam Pahel Meitei, Assistant Professor Dept. of Medicine

Srinivas Kulkarni, Consultant Physician

Arindam Chatterjee, Department of Health and Family Welfare, Government of West Bengal

Apurba Mukherjee, Ex-Head of Department of General Medicine and Acting Head

Avula Laxmaiah, NIN -Scientist

Ajay Kumar Singh, Consultant Internal Medicine & Cardio Diabetology

Vikas Bhutani, Director-Internal Medicine

Prabhat Goel, Consultant Physician

Sandeep Gupta, Consultant Physician

Puneet Saxena, Senior Professor of Medicine

Vikas Oswal, Chest Consultant, Chairperson

Ramesh Dargad, Honorary Cardiologist

Madhukar Rai, Professor and HOD Medicine

Suhas Gopal Erande, Consultant Physician

Parag Shah, Director

Nikhil Bangale, Head Medical Affairs, Consumer Health at Bayer

Cite this article: Mahesh M, Jaykrishnan B, Sudagani J, Mylapore SS, Bharti BB, Kumar Dhandhanian V, Pahel Meitei S, Kulkarni S, Chatterjee A, Mukherjee A, Laxmaiah A, Singh AK, Bhutani V, Goel P, Gupta S, Saxena P, Oswal V, Dargad R, Rai M, Erande SG, Shah P, Bangale N. Demystifying the micronutrient deficiency burden in India. *IP J Nutr Metab Health Sci* 2022;5(3):91-99.